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February 11, 2003

Select Agent Program
Centers for Disease Control and Prevention
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Regulatory Analysis and Development, PPD
APHIS
Station 3C71
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Re: Interim Final Rule on Possession, Use, and Transfer of Select Agents and Toxins, 67 Federal Register Volume 240 - 42 CFR 73, 42 CFR 1003; 7 CFR Part 331 and 9 CFR Part 121 (Docket No. 02-088-1)

I write on behalf of the University of California (UC) regarding the interim final rules on the possession, use, and transfer of select agents and toxins published by the Center for Disease Control and Prevention (CDC) and the Animal and Plant Health Inspection Service (APHIS) in the December 13, 2002, Federal Register. The UC system, comprised of ten research campuses and three national laboratories, conducts research utilizing hazardous biological agents and toxins designated as "select agents" under these regulations. Through our research on select agents and in many other scientific and technical fields, UC plays a critical role in contributing to our nation's fight against terrorism. I am grateful for the opportunity to communicate UC's general concerns regarding the proposed interim final rule and to provide detailed comments regarding issues presented by its specific provisions.

General Concerns Regarding the Proposed Interim Final Rule

As UC Santa Cruz Chancellor MRC Greenwood recently observed, "to preserve the university community's ability to provide key research that contributes to the future safety of our country, we should take care not to break what works well and not to attempt to fix what is not broken. As we consider and implement the interim proposed final rule and other regulations that change how select agent research is conducted, we should be mindful of the delicate balance that must exist between openness and security. We must take care not to tip the scales unnecessarily and thus risk the enormous benefits of a free and open environment in science and research."

UC is committed to implementing a responsible approach to securing hazardous agents and toxins, while ensuring that research requiring access to these hazardous materials by appropriately trained and screened persons may be conducted. We observe, however, that among the unintended consequences of the proposed interim final rule are the possible deleterious impacts on freedom of scientific information exchange and scientific inquiry, high financial costs of instituting security measures, and the possible loss to UC and other academic research institutions of foreign researchers and technical workers in areas of short supply among U.S. citizens. Many of the select agents currently are routine (and thus important) tools in research laboratories and are used in contexts that have nothing to do with

weapons. American biological and medical science might be significantly damaged because many scientists may in the end elect to avoid use of select agents despite their status as the best tool for a particular application, due to the scientists' perception that the regulatory burden on this type of research is simply too onerous. We fear that these rules are going to make it quite difficult to do biodefense research outside of a secured government facility.

The proposed interim final rule requires institutions possessing select agents to implement many new record-keeping procedures, training requirements and facility improvements and construction. We agree with the CDC and APHIS observations that these costs will be significant. The accelerated pace of implementing the inventory, security and training requirements under the proposed interim final rule impose an immediate financial burden that is, by our estimate, significantly greater than the average annualized cost ($153,000) estimated by the CDC. Systemwide, we estimate our first year costs at nearly $4 million, with annual maintenance costs thereafter of over $700,000.

We feel that, short of direct federal funding, an exemption of the administrative cost cap would be appropriate, if not essential, to ensure compliance. Any effort to recover costs of compliance through the traditional overhead cost mechanism will, in our view, result in a significant under recovery and under funding of costs. UC also requests that that new investigators establishing labs be eligible to receive funds to cover security costs as part of their start up grants packages. Established investigators beginning experimental programs using select agents should be encouraged to incorporate appropriate security costs in their grant proposals.

UC joins CDC and the APHIS in acknowledging that the various deadlines prescribed in the legislation create a shorter time frame than is ideal for developing the regulations. We request that those agencies do their utmost to ensure that those affected by the proposed interim final rule – scientists, academics, industrialists and the public -- are involved in what we hope will be an on-going process to refine these regulations.

Comments on Specific Provisions of the Proposed Interim Final Rule

CDC Section 73.1 and APHIS Section 331.1 Definitions- Responsible Official: UC requests that CDC and APHIS provide consistent definitions for "Responsible Official" (RO) in 7 CFR 331, 9 CFR 121 and 42 CFR 73. The APHIS regulations (7 CFR 331.1) define the RO as, "The individual designated by an entity to act on its behalf. This individual must have the authority and control to ensure compliance with the regulations in this part." There is no parallel provision in the CDC proposed interim final rule, and UC requests that the APHIS definition be inserted there at Section 73.1.

CDC Section 73.11 and APHIS section 331.10 Definitions- Access: UC requests that the CDC/APHIS rules be amended to clarify and make consistent the definition for access described in these two sections. The APHIS section states, "individuals who have a legitimate need *to handle or use* listed agents or toxins....". CDC section 73.1 is not as clear. Clarification is critical because record keeping requirements, as well as security and training costs for personnel depend on the scope of this term. UC joins the Howard Hughes Medical Institutes (HHMI), the Council On Governmental Relations (COGR), and others in requesting that the term "Access" be defined clearly as *the ability to gain physical control of select agents and toxins*. This change will make implementation of this rule somewhat less burdensome by limiting the scope of its application and reducing the number of applicants for clearances. This distinction will allow persons, including students and postdoctoral researchers, who conduct research on data or other information related to the select agent, but do not have or need physical access to that agent, to avoid unnecessary delays and carry on their research without a clearance.

CDC Section 73.4 (f)(2) select agents and toxins –Exclusions: UC requests that this provision be amended to define the "non-viable" and "non-functional" descriptors of select agents or toxins that would not be subject to the proposed interim final rule. Some organisms can survive in nature, others only with laboratory conditions, while others will not grow under any conditions.

CDC Section 73.7 Registration: The estimated number of background checks that the federal government will have to execute is estimated at 20,000 nationwide. It is very uncertain that the responsible federal agencies have the mechanisms in

place to process expeditiously this number of background reviews. Although the proposed rules make some allowances for the continuation of on-going select agent research while the background check process is underway, there is no accommodation for those who are "in the queue" with proposals to start such research. Further, the presence of a significant number of foreign researchers on most university and college campuses, including UC, makes it imperative that the DOJ be able to guarantee timely as well as accurate checks. The terms "expedited review" and "short term visit by a prominent researcher" should be more clearly defined as specific time frames. A delay in processing background checks will obviously result in a delay for initiating new research initiatives on select agents and toxins.

CDC Section 73.7(d) Protocol review: The proposed interim final rule requirement for information on protocols is not consistent with the draft application for registration documents that were distributed previously by CDC and USDA. UC observes that protocols, as defined in this section, can change frequently. Obtaining prior approval from HHS for changes in biosafety and laboratory information and objectives of work with select agents or toxins would result in delays that are likely to impede research. UC requests that the term, "protocols" be deleted from this subsection.

CDC Section 73.8 Security Risk Assessment: UC was a national leader in the effort to amend the "Bioterrorism Preparedness and Response Act of 2002" to include an administrative appeals provision for researchers who believed they were erroneously designated as "restricted persons," barred from access to select agents for bona fide research, education and other legitimate purposes. Unfortunately, the proposed interim final rule does not describe procedures by which the administrative appeals process would be implemented. Without this appeals process, researchers will have no expedited administrative recourse to dispute their erroneous designation as "restricted persons." We anticipate that legitimate appeals are likely to arise, whether based upon federal database entry errors or other clerical mistakes, a federal agency's misapplication of law, or instances where a federal law enforcement agency may mischaracterize their suspicions of the appellant's engagement terrorism as "reasonable." Without an expedited appeals process that is required to redress such errors in a short and specific timeframe, critical research may be delayed unreasonably or stopped entirely.

UC requests that the proposed interim final rule be amended to include a description of an expedited appeals process with specific timelines, and if HHS makes a determination to deny an individual access to select agents, that individual should receive from HHS a notice of the reasons for such denial.

UC requests that the proposed interim final rule be amended to provide that if the person subject to the background check suffers a delay in excess of 10 work days, that person should be permitted to work with select agents under the direct supervision of an approved person (provided that all other requirements are met).

UC, as the administrator for three national DOE laboratories, requests that language be added to this section that would allow the L or Q clearance granted in DOE laboratories (or equivalent) to be considered synonymous with the security risk assessment process for the purposes of this regulation and that individuals with a current L or Q clearance be considered approved.

UC is deeply concerned that the registration information, whether submitted by UC or collected through the DOJ background check, will be used more broadly than to determine who is a "restricted person" ineligible to conduct research. UC policy and California State law (the California Information Practices Act) prohibit discrimination in employment based upon citizenship. These authorities also prohibit us from disclosing citizenship information to a third party in a manner that links that information to an individual, except in limited and compelling circumstances. It has been our practice historically not to make exceptions to that general rule. Our rationale is that university

researchers should be selected for participation on projects on the basis of merit and ability to contribute to the research project. Research support staff are selected on the same basis. Students, faculty and staff from abroad who are not U.S. citizens make a major contribution to the conduct of research at UC.

The proposed interim final rule language does not describe the information that must be submitted by the entity regarding individuals with access to select agents, nor does it describe procedures HHS and USDA must follow to limit the use of data collected in the course of the registration process. UC requests that the proposed interim rule prohibit HHS, USDA or other federal agencies from using the information collected through the registration process to evaluate the merit of proposals involving research on select agents or toxins.

The data that will be collected in the course of the background checks in the registration process will include citizenship status and other information that might not disqualify a person from select agent research, but might be used inappropriately by a federal agency to assess a proposal for funding.

UC requests new language in this provision to require that the Departments of Justice (DOJ), Health & Human Services (HHS) and Agriculture (USDA) ensure the security and confidentiality of required registration information that is personal or classified. It is key that the data collected in the registration process to determine the eligibility of persons to have access to select agents and toxins not be used as factors in determining the merit of research proposals submitted by those persons.

CDC Section 73.10 (c) Safety - An entity may not conduct the following experiments unless approved by the HHS Secretary after consultation with experts: This provision requires prior approval from the Department of Health and Human Services for genetic engineering experiments that might make a select agent more toxic or more resistant to known drugs. UC recognizes that the experiments defined in this subsection (Recombinant-DNA experiments that enhance drug resistant traits to select agents and Recombinant-DNA experiments involving formation of more lethal toxins) can be very dangerous and should be regulated. We request that the NIH Recombinant Advisory Committee (RCA) be designated to review these sensitive experiments and that NIH fund RCA to process the anticipated high volume of protocols so that biodefense research can quickly ramp up to full throttle. UC researchers would not wish to be even one day late in delivering the breakthroughs that will be needed.

UC's researchers utilize deliberate formation of antibiotic resistance as a common research tool. If strictly imposed, subsection 73.10(c) would limit this standard research practice. An example of an antibiotic resistance application: Transposon insertion libraries are common experimental creations used to generate gene knockouts and study the effect on expression and phenotype. However, this often results in an array of genomes containing antibiotic resistance markers used for selection and screening. The method is common enough not to need approval from a cabinet level position and too burdensome if approval is needed for each of several thousand insertional mutants that would be created for a single genome.

In regard to this subsection's language incorporating the "Biosafety in Microbiological and Biomedical Laboratories" and the "NIH Guidelines for Research Involving Recombinant DNA Molecules," we agree with the recommendation made by HHMI, that the HHS Secretary not incorporate these guidelines as requirements in the final regulations. We recommend that the final regulations recognize these guidelines as authoritative codes of practice that entities should consider in developing and implementing a performance-based safety plan for the safe possession and use of select agents.

CDC Section 73.11 Security: UC recommends that this subsection, which requires that the security plan be reviewed by the Responsible Official at least annually and after any incident, be rephrased to be consistent with 7 CFR Part 331 and 9 CFR Part 121 that state, "(The Security) Plan must be reviewed, performance tested, and updated annually." UC also requests that, where laboratories are used intermittently for select agent research, free access be

permitted when select agents and toxins are in not in use and when the select agents and toxins are secured in a safe or other secured storage.

UC-managed national laboratories already have most of the security infrastructure in place to comply with the physical security, record keeping and other security plan requirements under this subsection. However, our campus laboratories will require some time to install security devices and barriers and to hire and train staff to administer the record keeping and inventory requirements under this provision. UC requests that the implementation date for the record keeping requirements

specified at HHS Section 73.0(a)(1) and 331.0 be changed to provide additional time for compliance and to coincide with the September 12, 2003, date for implementation of the security plan required under HHS Section 73.11 and USDA Section 331.11.

UC also believes that our ability to implement the security plan required under this provision would be aided greatly by the clarification of certain terms used to describe security controls, specifically, the words "area" and "access."

UC seeks to clarify the definition of "area" because our laboratories are in some cases large and house many different researchers working on a variety of projects, only a few of which might include utilization of select agents or toxins. Under this subsection, the entire lab would be subject to physical security requirements and access restrictions that would be inappropriate for scientists and workers who are not engaged in select agent research. We believe that the regulation should be flexible enough to allow local solution of this issue. This could be achieved by allowing the entity to designate some portion of the lab as a select agent area for which use and entry restrictions would be governed by these select agent regulations.

UC seeks also to clarify the definition of "access." In our large multi-use labs, select agents will be under direct supervised control of registered persons while in use and securely stored when not in use. In our view, there would be little gained in terms of security to require access control, specialized safety training, and personnel background checks of others who share that large multi-purpose lab space. If everyone in these large multi-use labs is required to meet the same training, background checks and record keeping requirements imposed on select agent researchers, the administrative burden would be great, the cost of duplicate equipment high, and the loss of collaborative research opportunities incalculable.

CDC Section 73.13 Training: We view the description of the required training on security as unclear. Depending upon the select agent or toxin being utilized, the Bloodborne Pathogen Training specified for use in the handling of all select agents and toxins in this proposed provision might not be sufficient in every instance. UC recommends that this section be revised to require training that is geared to the select agent being utilized and the level of an individual's access to select agents and toxins.

CDC Section 73.14 Section Transfers: UC views this subsection's requirement that CDC or APHIS approve each select agent or toxin transfer between entities as highly likely to produce unreasonable delays. This is especially true for the UC system, which includes nine R1 campuses and many intercampus research programs. UC supports a requirement that CDC/APHIS receive immediate notification of each transfer. If CDC/APHIS must authorize every transfer, UC requests that these regulations be revised to require CDC/USDA to respond within an appropriate interval, e.g., 1-2 business days. UC also requests that a quarterly reporting requirement for the notification of consumption or destroying the select agent or toxin be substituted for the proposed interim rule's five business days notification requirement because the latter constitutes an unrealistic burden.

HHS Section 73.15 Records: It will be difficult to maintain real time/current records of (c)(1) and (2) for internal transfers of select agents until badge readers or bar code readers (with data accessible by the RO) are installed for each laboratory and for each storage area (Please see our comments on HHS Section 73.11 Security, above, requesting a September 12, 2003 implementation date for these requirements). Until we are able to install these

access controls, we request flexibility regarding access control and have already directed our Principal Investigators to be accountable for implementing other security measures such as locked doors and locked freezers.

CDC Section 73.17(d) Notification of theft, loss or release: This subsection requires notification of HHS Secretary and State or local public health agencies of any "release outside of the primary containment barriers." To some, this would mean outside the biological safety cabinet, and to others it means the laboratory. We recommend that a spill/release notification be required only outside the laboratory room designated for this work.

CDC Section 73.21 Draft Report Forms: UC requests that the below-specified report forms be modified as noted:

REPORT OF THE IDENTIFICATION OF SELECT BIOLOGICAL AGENTS AND TOXINS FROM CLINICAL OR DIAGNOSTIC LABORATORIES (draft form) This form does not provide for Responsible Office (RO) verification of the information requested and should be modified to reflect that the RO has reviewed and approved the form.
REQUEST FOR EXEMPTION OF SELECT BIOLOGICAL AGENTS AND TOXINS OR HIGH CONSEQUENCE LIVESTOCK PATHOGENS AND TOXINS (draft form) Same comment as above.
REPORT OF THEFT, LOSS, OR RELEASE OF SELECT BIOLOGICAL AGENTS AND TOXINS (draft form)
This form should be modified to specify "UNINTENTIONAL" release in the guidance and the title.
APPLICATION FOR LABORATORY REGISTRATION - APHIS FORM 2044/CDC FORM 0.1319
This form should be revised to require that the Principal Investigator sign a certification form similar to the ROs - for maintaining inventory, certifying lab skills, controlling access (giving training to unauthorized personnel, determining legitimate need for access for authorized personnel), and reporting theft, loss, or release.
REPORT OF IDENTIFICATION OF SELECT BIOLOGICAL AGENTS AND TOXINS FROM CLINICAL OR DIAGNOSTIC LABORATORIES - APHIS Form 2040/CDC Form 0.1318 - This form's Introduction, last paragraph, "...or transferred to a registered entity/facility..." – should be revised to be consistent with regulation section 73.6(a)(4), "to a facility eligible of receiving them." This revision is necessary because the current language leaves open the possibility of transfers to any registered entity rather than to one that is approved for the specific select agent or toxin. This form does not provide for Responsible Office (RO) verification of the information requested if a select agent or toxin is reported and should be modified to reflect that the RO has reviewed and approved the information reported

UC has reviewed the comments submitted by the Association of American Universities, the Council on Governmental Relations and the Howard Hughes Medical Institute, and endorses their views on the proposed interim final rule.

Thank you for the opportunity to comment on the proposed interim final Rule on Possession, Use, and Transfer of Select Agents and Toxins.

Sincerely,

Lawrence B. Coleman
Vice Provost for Research

Cc: President Atkinson
Provost King
Vice President Mullinix
Vice President Drake
Interim Director Hall

Re: Interim Final Rule on Select Agents and Toxins February 11, 2003

Bcc: Director Mears
Interim Director Auriti